

In re Appln. of Crystal et al.
Applicati n No. 09/629,074

CLAIM AMENDMENTS

1. (Currently amended) A method for enhancing bone density or formation, the method comprising administering to at least one first cell within a bone or within a tissue immediately surrounding a bone an adenoviral vector comprising ~~associated with a region of a bone~~ at least one first nucleic acid encoding a vascular endothelial growth factor, such that the first nucleic acid is expressed in the cell to produce the vascular endothelial growth factor, whereby bone density or formation is enhanced within the region, ~~wherein the first cell is within the bone or within a tissue immediately surrounding the bone.~~

2. (Currently amended) The method of claim 1, wherein ~~at least one of the nucleic acids~~ the adenoviral vector is exposed to at least one cell in vivo in the region of the bone.

3. (Currently amended) The method of claim 1, wherein ~~at least one of the nucleic acids~~ the adenoviral vector is exposed to at least one cell ex vivo, which is then delivered in vivo to the region of the bone.

4. (Previously amended) The method of claim 1, wherein the vascular endothelial growth factor is VEGF121.

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5. (Previously amended) The method of claim 1, wherein the vascular endothelial growth factor is selected from the group consisting of VEGFA138, VEGFA162, VEGF182, VEGF189, VEGF2, and VEGF-C.

6. (Currently amended) The method of claim 1, further comprising administering to at least one second cell within the bone or within a tissue immediately surrounding the bone an adenoviral vector comprising ~~associated with the region~~ at least one second nucleic acid encoding at least one osteogenic protein, such that the second nucleic acid is expressed in the cell to produce the osteogenic protein, ~~wherein the second cell is within the bone or within a tissue immediately surrounding the bone.~~

7. (Previously amended) The method of claim 6, wherein the osteogenic protein is selected from the group consisting of a bone morphogenic protein (BMP), a transforming growth factor (TGF), a latent TGF binding protein (LTBP), latent membrane protein-1 (LMP-1), a heparin-binding neurotrophic factor (HBNF), growth and differentiation factor-5 (GDF-5), a parathyroid hormone (PTH), a fibroblast growth factor (FGF), an epidermal growth factor

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(EGF), a platelet-derived growth factor (PDGF), an insulin-like growth factor, a growth factor receptor, a cytokine, a chemotactic factor, a LIM mineralization protein (LMP), a leukemia inhibitory factor (LIF), a hedgehog protein, and midkine (MK).

8. (Original) The method of claim 6, wherein the osteogenic protein is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 and BMP-8.

9. (Original) The method of claim 6, wherein the osteogenic protein is TGF- β 1.

10. (Original) The method of claim 6, wherein the osteogenic protein is BMP-2.

11. (Original) The method of claim 6, wherein the osteogenic protein is MK.

12. (Original) The method of claim 6, wherein the osteogenic protein is HBNF.

13.-16. (Previously cancelled)

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18. (Previously amended) The method of claim 6, wherein the first nucleic acid and the second nucleic acid are the same nucleic acid.

19. (Currently amended) ~~A viral~~ An adenoviral vector comprising at least one first nucleic acid encoding a vascular endothelial growth factor and at least one second nucleic acid encoding at least one osteogenic protein.

20. (Cancelled)

21. (Original) The ~~viral~~ adenoviral vector of claim 19, which is deficient in at least one essential gene function.

22. (Previously amended) A bone graft comprising at least one first cell having at least one first exogenous nucleic acid encoding a vascular endothelial growth factor and at least one second cell having at least one second nucleic acid encoding at least one osteogenic protein.

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23. (Previously amended) The bone graft of claim 22, wherein the osteogenic protein is selected from the group consisting of a bone morphogenic protein (BMP), a transforming growth factor (TGF), a latent TGF binding protein (LTBP), latent membrane protein-1 (LMP-1), a heparin-binding neurotrophic factor (HBNF), growth and differentiation factor-5 (GDF-5), a parathyroid hormone (PTH), a fibroblast growth factor (FGF), an epidermal growth factor (EGF), a platelet-derived growth factor (PDGF), an insulin-like growth factor (IGF), a growth factor receptor, a cytokine, a chemotactic factor, a LIM mineralization protein (LMP), a leukemia inhibitory factor (LIF), a hedgehog protein, and midkine (MK).

24. (Previously cancelled)

25. (Previously amended) The bone graft of claim 22, which is an allograft.

26. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the vascular endothelial growth factor is VEGF121.

E1 27. (Previously added) The bone graft of claim 22, wherein the vascular endothelial growth factor is VEGF121.

28. (Previously added) The bone graft of claim 22, wherein the vascular endothelial growth factor is VEGF165.

29. (Previously added) The bone graft of claim 22, wherein the osteogenic protein is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 and BMP-8.

30. (Previously added) The bone graft of claim 22, wherein the osteogenic protein is TGF- β 1.

31. (Previously added) The bone graft of claim 22, wherein the osteogenic protein is BMP-2.

32. (Previously added) The bone graft of claim 22, wherein the osteogenic protein is MK.

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33. (Previously added) The bone graft of claim 22, wherein the osteogenic protein is HBNF.

34. (Cancelled)

35. (Cancelled)

36. (Previously added) The method of claim 1, wherein the vascular endothelial growth factor is VEGF165.

37. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the vascular endothelial growth factor is VEGF165.

E) 38. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is selected from the group consisting of a bone morphogenic protein (BMP), a transforming growth factor (TGF), a latent TGF binding protein (LTBP), latent membrane protein-1 (LMP-1), a heparin-binding neurotrophic factor (HBNF), growth and differentiation factor-5 (GDF-5), a parathyroid hormone (PTH), a fibroblast growth factor (FGF), an epidermal growth factor (EGF), a platelet-derived growth factor (PDGF), an insulin-like growth factor, a growth factor receptor, a cytokine, a chemotactic factor, a LIM mineralization protein (LMP), a leukemia inhibitory factor (LIF), a hedgehog protein, and midkine (MK).

39. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 and BMP-8.

40. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is TGF- β 1.

41. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is BMP-2.

42. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is MK.

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43. (Currently amended) The ~~viral~~ adenoviral vector of claim 19, wherein the osteogenic protein is HBNF.
